likely to be much higher because of actual under-reporting (appendix).[6,7] The geographical spread of the cases reported in 2019 affects all districts of the country, exhibits a clear predominance in men (64·11% for men *vs* 35·89% for women), and primarily encompassed younger adults (whereby people aged 15–35 years accounted for 51·42% of 29 855 total cases).[6]

As national surveillance is passive and only government hospitals are included, it is highly likely that substantial under-reporting is taking place. Furthermore, the operational surveillance is not based on appropriate methods, such as the WHO projection done in July, 2019, where an estimated 358 960 people were deemed to be infected compared with only 7179 cases in official reports.[8] Based on the aforementioned official number of cases in November, 2019, as many as 3–4 million people could have conceivably been infected.

We cannot underscore the seriousness of the current epidemic, which is unfortunately being handled with great laxity by the country's authorities, as shown not only by the marked under-reporting, but also by the absence of health awareness campaigns targeting both the general public and health professionals. Such campaigns that aim for earlier and more consistent recognition and supportive clinical management of dengue cases are a major factor underlying reduced mortality for this highly contagious disease, and are urgently needed.[2]

We declare no competing interests.

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The dengue epidemic and climate change in Nepal

Climate change is affecting the incidence of dengue infections spread by two species of *Aedes* mosquitoes: *Aedes aegypti* and *Aedes albopictus*. The vectors of dengue and other arboviruses, including chikungunya, Zika virus, and yellow fever, depend on temperature and precipitation for their growth, survival, and feeding behaviour.[1] Dengue transmission is highly sensitive to temperature, which affects generation time, the elapsed period from one cycle of vector-to-human transmission to the start of a new cycle.[2] The epidemic potential is described by vectorial capacity using compartmental models of the disease transmission processes. In the 2018 *Lancet* climate Countdown report,[3] global vectorial capacity for the transmission of the dengue fever virus was reported as the highest on record, rising to 9·1% for *A aegypti* and 11·1% for *A albopictus,* more than the 1950s baseline.

In Nepal, the Global Circulation Model outputs suggest that overall temperatures will increase between 0·5°C and 2·0°C by the 2030s and between 3·0°C and 6·3°C by the 2090s.[4] One estimate suggests that the average annual maximum temperature of Nepal has risen by 0·056°C over the past 40 years, with greater warming at higher altitudes.[5] Dengue fever was first reported in Nepal in 2004.[6] Since then dengue cases have been reported every year with circulation of all four serotypes. In 2018 a total of 3425 cases with one death were reported.

In 2019, Nepal saw unexpected early rains—starting in late March. Normally the monsoon season starts by June and lasts for about 3 months, but in 2019 monsoons entered Nepal in the third week of June and a month later the country received the heaviest rainfall for a decade.[7] Starting on July 11, 2019, incessant rainfall for a week triggered flooding and landslides in many areas, especially in southeastern districts of the country. The Bagmati and Kamala river basins experienced extreme amounts of rainfall, and Kathmandu and eastern Nepal were hit by severe flooding. The first dengue fever case was reported on May 13, 2019, from the Sunsari district in the east of the country followed by Makwanpur, southwest of Kathmandu, on July 27, 2019. The outbreak then spread like wildfire reaching 68 out of 77 districts over the next 2 months. Efforts to destroy mosquito breeding sites began but devolution under the new federal system meant the responsibilities of local actors were unclear.

As of late September, 2019, more than 10 000 cases of dengue fever and six deaths were officially reported by the Epidemiology and Disease Control Division, Ministry of Health, Kathmandu, Nepal. However, we believe these reported figures greatly

underestimate the size of the epidemic. The Sukraraj Tropical and Infectious Disease Hospital in Kathmandu, Nepal, is the only national centre for infectious diseases in the country. In the Kathmandu Valley, several thousand cases were detected using the rapid diagnostic test combo kit (which includes non-structural protein 1, IgM, and IgG). Only patients suspected of having dengue with a platelet count of less than 100 000 and white blood cell count of less than 4000 were tested with the rapid diagnostic test combo kit. We received more than 13 000 patients suspected to have dengue and tested only 5000 cases, of which 40% were positive for dengue infection over a 10 day period. 14 staff from the hospital tested positive.

Dengue fever in Nepal, as in many parts of south Asia, is now an annual epidemic, and with a changing climate dengue presents a growing threat to Nepalese nationals and foreigners. The US Government has already warned people not to visit Nepal during this dengue epidemic. Potential alarm indicators for climate (eg, temperature, rainfall, and humidity) and vector presence or density could be useful to predict outbreaks and minimise their effect. Next year the country celebrates Visit Nepal 2020, so the costs of infectious diseases exacerbated by human-induced climate change present a growing menace to Nepal's economy.

We declare no competing interests.

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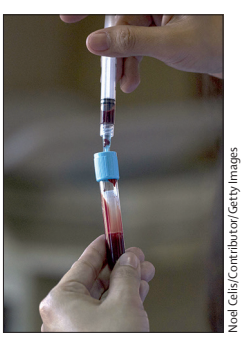
Vaccine-attributable severe dengue in the Philippines

In 2016, WHO[1] recommended that the dengue vaccine CYD-TDV (Dengvaxia; Pasteur, Lyon, France), the first dengue vaccine, licensed for use in adults and children aged 9 years or older, be considered for use in highly endemic regions where at least 70% of 9-year-old children had previously been infected with dengue. The Philippines was the first country to introduce Dengvaxia on a large scale in selected highly endemic regions, targeting about 1 million children aged 9–10 years. In November, 2017, an excess risk of hospitalisation for dengue and severe dengue in vaccinees who had not had a previous dengue infection at the time of vaccination was reported,[2] on the basis of retrospective analyses[3] of data from the Dengvaxia phase 3 trials, using a novel non-structural protein 1 (NS1) based antibody assay. Following a reanalysis of these data,[3] the Philippine Dengvaxia programme was suspended. However, by the time the programme had been suspended, more than 830 000 children had received at least one of the three recommended Dengvaxia doses. The news about the safety concerns in dengue-naive vaccinees led to major public outcry, with loss in vaccine confidence that extended to routine childhood vaccines.[4]

Parents whose children had received Dengvaxia were understandably alarmed by the reported adverse effect of the vaccine, especially because most parents will not have known whether their child had been infected by the dengue virus previously, and any cases of severe dengue in vaccinees might have been attributed to the disease-enhancing properties of the vaccine in seronegative children. Similarly, clinicians looking after vaccinated children admitted with severe dengue were also tempted to attribute every episode to vaccine-enhanced disease. However, in reality a minority of cases are likely to be attributed to vaccine-enhanced disease.



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No vaccine is 100% efficacious and cases of breakthrough disease arise through vaccine failure. For the first licensed dengue vaccine, the issues of efficacy and safety are complex because both are driven by serostatus. Serostatus refers to whether a person has had a previous dengue infection; a seropositive person will have had at least one dengue infection in the past, whereas a seronegative person is dengue-naive. The efficacy of Dengvaxia against severe dengue in seropositive vaccinees in the phase 3 trials was 84% (95% CI 63–93).[3] Most vaccinees in the Philippine programme, possibly around 85%, were likely seropositive.[5] Hence, we would expect to see breakthrough disease in seropositive vaccinees when exposed to natural infection, especially in light of the current outbreak of dengue in the Philippines. Cases of severe dengue would be a mixture of breakthrough cases and of enhanced disease in seronegative children.[6]

The risks associated with Dengvaxia must be put into perspective. First, many cases of hospitalisation and severe dengue following vaccination are likely to be attributable to vaccine breakthrough cases in seropositive vaccinees because a high proportion of vaccinees are dengue seropositive, in whom the vaccine protects but does not give total protection. Second, in